Restricted diffusion in benign CNS neoplasms: imaging pitfalls and histopathological correlations

Poster No.: C-1968
Congress: ECR 2012
Type: Educational Exhibit
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Keywords: Pathology, Neoplasia, Imaging sequences, Comparative studies, MR-Diffusion/Perfusion, Neuroradiology brain
DOI: 10.1594/ecr2012/C-1968

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Learning objectives

The purpose of this exhibit is to demonstrate:

- MR imaging of various benign central nervous system (CNS) neoplasms with diffusion restriction, low apparent diffusion coefficient (ADC) values, and their histopathological correlations.
- DWI and ADC values may be useful in characterizing and grading benign CNS tumors.

The content will be organized and presented in the following manner using the World Health Organization (WHO) classification of CNS tumors:

I. Tumors of neuroepithelial tissue

A. Astrocytic tumors
   1. Pilocytic astrocytoma (WHO grade I)
   2. Pleomorphic xanthoastrocytoma (WHO grade II)
   3. Diffuse astrocytoma (WHO grade II)

B. Choroid plexus tumors
   1. Choroid plexus papilloma (WHO grade I)
   2. Atypical choroid plexus papilloma (WHO grade II)

C. Neuronal and mixed neuronal-glial tumors
   1. Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)
   2. Desmoplastic infantile ganglioglioma (WHO grade I)
   3. Ganglioglioma (WHO grade I)
   4. Central neurocytoma (WHO grade II)

D. Tumors of the pineal region
   1. Pineocytoma (WHO grade I)
   2. Papillary tumor of the pineal region (WHO grade II, III)

II. Tumors of the meninges

A. Tumors of meningotheelial cells
   1. Meningioma
• Meningothelial or benign meningioma (WHO grade I)
• Microcystic meningioma (WHO grade I)
• Atypical meningioma (WHO grade II)

B. Mesenchymal tumors

   1. Hemangiopericytoma (WHO grade II)

III. Tumors of the sellar region

A. Pituitary Adenoma

Background

Diffusion-weighted imaging (DWI) technique has many useful applications within brain MR imaging, especially when it comes to differentiating between neoplasms, infection, and stroke.

DWI and corresponding ADC values are helpful in differentiating the cellularity, nuclear-to-cytoplasm ratio, and extracellular matrix of neoplasms, which ultimately help in their characterization and grading.

• High-grade CNS tumors often demonstrate diffusion restriction and decreased ADC values due to their high tumor cellularity, increased nuclear-to-cytoplasm ratio, and decreased extracellular matrix volume.

• However, various benign CNS neoplasms also demonstrate restricted diffusion also suggesting increased cellularity.

Using the World Health Organization (WHO) classification of tumors of the central nervous system, we demonstrate characteristic findings of several benign CNS neoplasms using DWI with focus on imaging pitfalls and histopathological correlations.

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A. Astrocytic tumors

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D. Tumors of the pineal region

1. Pineocytoma (WHO grade I)
2. Papillary tumor of the pineal region (WHO grade II, III)

II. Tumors of the meninges

A. Tumors of meningothelial cells

1. Meningioma
   - Meningothelial or benign meningioma (WHO grade I)
   - Microcystic meningioma (WHO grade I)
   - Atypical meningioma (WHO grade II)

B. Mesenchymal tumors

1. Hemangiopericytoma (WHO grade II)

III. Tumors of the sellar region

A. Pituitary Adenoma

Imaging findings OR Procedure details

I. Tumors of neuroepithelial tissue

A. Astrocytic tumors
1) Pilocytic astrocytoma (WHO grade I)

- Common CNS tumor of mid-childhood that presents in the cerebellum or suprasellar region.
- It has a solid hypercellular component that one would expect to show hyperintensity on diffusion weighted imaging (DWI).
- However, due to its rich extracellular matrix and cystic/necrotic components it often demonstrates isointensity on diffusion and high signal on ADC map of greater than $1.5 \times 10^{-3}$ mm$^2$/s. (Fig. 1 on page 9)

Important Learning Points:

- Hypercellular tumors often demonstrate increased restricted diffusion. However, factors such as abundant extracellular matrix may offset diffusion hyperintensity and instead show isointensity on diffusion with increased ADC value. DW isointensity and increased ADC due to the balance between increased diffusibility and T2 hyperintensity is known as T2 washout.
- The extracellular matrix (ECM) is composed of fibrous proteins and glycosaminoglycans.
- A study by Sadeghi et al has shown high levels of a specific type of highly hydrophilic glycosaminoglycan called hyaluronan or hyaluronic acid expressed in astrocytic tumors. This is believed to cause shifting of large amounts of water and thus affect the value of ADC.

2) Pleomorphic xanthoastrocytoma (WHO grade II)

- A cortically based astrocytic tumor in younger patients often less than 30 years of age.
- It is often associated with epilepsy and can have malignant transformation.
- The case in Fig. 2 on page 9 shows a solid mass with surrounding cystic components.
- The DW hyperintensity and slightly low ADC values is most likely due to hypercellularity.

Important Learning Points:

- Various low-grade CNS neoplasms demonstrate hypertensity on DW images and low ADC values most likely due to the hypercellular composition of the tumors.

3) Diffuse astrocytoma (WHO grade II)

- 2nd most common astrocytoma of childhood after pilocytic astrocytoma. More often occurs in adults.
• Usually does not show gadolinium enhancement or diffusion restriction.
• The example in Fig. 3 on page 11 shows increased IV contrast enhancement suggesting higher grade. This is an unusual case of mild DWI hyperintensity and slightly low ADC value. Most low grade astrocytomas demonstrate elevated ADC.

B. Choroid plexus tumors

1) Choroid plexus papilloma (WHO grade I)
2) Atypical choroid plexus papilloma (WHO grade II)

• Intraventricular papillary neoplasm derived from choroid plexus epithelium
• Often occurs in young children
• Atypical entity is known for its increased mitotic activity.
• Fig. 4 on page 11 shows an intraventricular lesion with DW hyperintensity and mildly increased ADC. The mass is hyperintense on T2 weighted image.

Important Learning Points:

• Diffusion weighted image has inherent T2 weighted component.
• DWI hyperintensity can be due to increased T2 prolongation or T2 shine-through.
• If T2, DWI, and ADC are all increased, then this is due to T2 shine-through.
• If DWI signal is increased and ADC is decreased, then this is true restricted diffusion.

C. Neuronal and mixed neuronal-glial tumors

1) Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)

• Rare condition of the cerebellum of neoplastic or malformation origin. (Fig. 5 on page 12)
• Associated with Cowden syndrome with increased risk of thyroid, breast, colon, and renal cancers.
• DWI shows hyperintensity, mildly increased ADC, and high T2 signal. Hypercellularity of ganglion cells replace the granular and Purkinje cells.
• Although rare, there have been cases of Lhermitte-Duclos that show low ADC.

2) Desmoplastic infantile ganglioglioma (WHO grade I)

• Large solid and cystic cortically based mass that occurs in young children. (Fig. 6 on page 13)
• DWI hyperintensity and decreased ADC is due to hypercellularity and/or decreased volume of extracellular matrix.

3) Ganglioglioma (WHO grade I)
• Most often a cortically based solid nodule with cystic component. (Fig. 7 on page 14)
• Associated with temporal lobe epilepsy

4) Central neurocytoma (WHO grade II)
• Benign lobular mass usually seen in the lateral ventricle with attachment to the septum pellucidum.
• DWI hyperintensity and decreased ADC is due to marked hypercellularity as seen in Fig. 8 on page 16.

D. Tumors of the pineal region

1) Pineocytoma (WHO grade I)
• Solid/cystic mass with peripheral calcifications in the pineal region.
• Shows avid gadolinium enhancement with restricted diffusion and decreased ADC. (Fig. 9 on page 16)

2) Papillary tumor of the pineal region (WHO grade II, III)
• Avidly enhancing pineal mass with solid/cystic components
• DWI hyperintensity and low ADC correlate with the hypercellularity as seen in Fig. 10 on page 17.

II. Tumors of the meninges

A. Tumors of meningothelial cells

1) Meningothelial or benign meningioma (WHO grade I)
• Most common extraaxial brain tumor. Meningothelial histologic subtype is benign grade I.
• DWI hyperintensity and low ADC is seen in Fig. 11 on page 18.

Important Learning Points:
• According to Kono et al and Yamasaki et al, there is no clear correlation between ADC values and the various histologic subtypes of meningiomas.
• No statistically significant difference was observed between benign and malignant meningiomas. However, it appears that malignant or atypical
meningiomas tend to have increased DW signal and low ADC values due to hypercellularity.

- However, large studies are required for definitive conclusions.

2) Microcystic meningioma (WHO grade I)

- A low-grade extraaxial CNS neoplasm with solid and cystic components.
- **Fig. 12** on page 19 shows an enhancing mass with a large central portion that restricts on diffusion with slight hypointensity on ADC. The peripheral microcystic region has hypointensity on DWI and increased ADC.

3) Atypical meningioma (WHO grade II)

- Higher grade of meningioma with slightly higher rate of recurrence than typical meningiomas after resection.
- **Fig. 13** on page 20 shows an heterogeneous mass with variable DWI and ADC signals. Focal areas of DWI hyperintensity and low ADC suggest increased cellularity, mitotic activity, and high nucleus to cytoplasmic ratio.

B. Mesenchymal tumors

1) Hemangiopericytoma (WHO grade II)

- Hypercellular and hypervascular extraaxial mass derived from vascular pericytes.
- Similar appearance to meningioma but without calcifications or hyperostosis.
- DWI shows mild hyperintensity and low ADC consistent with its hypercellularity and dense interstitium. (**Fig. 14** on page 22)

III. Tumors of the sellar region

A. Pituitary Adenoma

- One of the most common benign sellar/suprasellar masses in adults.
- Macroadenomas defined by >10mm; microadenoma are <10mm.
- Most are endocrinologically active. Rest are non-functioning adenomas.
- DWI hyperintensity and low ADC suggestive of hypercellularity is seen in **Fig. 15** on page 22.

Miscellaneous

A. Epidermoid cyst

- Benign tumor of ectodermal origin with stratified squamous epithelium and keratinaceous debris.
• Often seen in the cerebellopontine angle (CPA) and 4th ventricle.
• Diffusion shows hyperintensity caused by both increased T2 and restricted diffusion. (Fig. 16 on page 23)
• Most epidermoids demonstrate mildly increased ADC secondary to T2-shine through, but the example in Fig. 16 shows iso- and hypointensity on ADC.

Images for this section:

![Fig. 1](image_url):
Hypothalamic pilocytic astrocytoma in a 5-year-old boy with headache. (a) T2-weighted image shows a hyperintense mass in the hypothalamus. (b) Gadolinium-enhanced T1-weighted image shows enhancement in the mass. c DW image shows isointensity. (d) ADC map shows hyperintensity in the mass (1.53×10^-3 mm²/s). (e) Pathology shows intermediate cellularity and abundant extracellular matrix (Rosenthal fibers and microcystic changes)
Fig. 2: Pleomorphic xanthoastrocytoma in a 36-year-old woman. (a) T2-weighted image shows a hypointense solid mass (arrow) with surrounding cystic components in the left frontoparietal region. (b) Gadolinium-enhanced T1-weighted image with fat saturation shows intense enhancement in the solid component. (c) DW image shows slight hyperintensity in the solid mass (arrow) and hypointensity in the cystic components. (d) ADC map shows isointensity in the solid component (0.70-0.94×10^-3 mm2/s). (e) FA is partially increased in the solid component (arrow). (f) Pathology shows cellular pleomorphism and hypercellularity.

Fig. 3: Diffuse Astrocytoma in a 4 month old infant. (a) Gadolinium-enhanced T1-weighted image with fat saturation shows intense enhancement in the solid component. (b) DWI shows mild diffusion restriction in the intraventricular lesion. (c) ADC map with slightly decreased value of 0.8×10^-3 mm2/s.
**Fig. 4:** Atypical choroid plexus papilloma in a 6-year-old girl. (a) Gadolinium-enhanced T1-weighted image shows heterogeneous enhancement of the mass. (b,c) T2-weighted and FLAIR images show a hyperintense mass in the occipital horn with surrounding edema suggesting brain parenchymal invasion. (d,e) DW image shows hyperintensity with slightly increased ADC in the mass.
Fig. 5: Lhermitte-Duclos disease in a 48-year-old woman. (a,b) T1- and T2-weighted images show a well-circumscribed mass with a striated pattern. (c) Gadolinium-enhanced T1-weighted image shows minimal vascular enhancement in the mass. (d,e) DW imaging shows a hyperintense mass associated with slightly increased ADC that may reflect an increased number and size of ganglion cells replacing the granular and Purkinje cell layers.
Fig. 6: Desmoplastic infantile ganglioglioma in a 5-year-old girl. (a) T2-weighted image shows an isointense solid mass (arrow) with a large cystic component. (b) Gadolinium-enhanced T1-weighted image shows a homogeneous enhancement in the solid portion of the mass. (c,d) DW imaging shows hyperintensity with partially decreased ADC in the solid portion of the mass.
**Fig. 7:** Ganglioglioma in a 31-year-old man with seizures. (a) T2-weighted image shows a well-defined mildly hyperintense lesion in the right parietal cortex (arrow). (b) Gadolinium-enhanced T1-weighted image with fat saturation shows heterogeneous enhancement (arrow). (c) DW image shows hyperintensity in the lesion. (d) ADC map shows isointensity in the lesion (0.76-0.88×10^-3 mm²/s; arrow). (e) Pathology shows intermediate cellularity composed of ganglion cells and neoplastic astrocytes.

![Fig. 7: Ganglioglioma](image)

**Fig. 8:** Central neurocytoma in 32-year-old woman. (a) Coronal T2-weighted image shows isointense intraventricular mass with cystic components involving the septum pellucidum (arrow). (b) Gadolinium-enhanced T1-weighted image with fat saturation shows heterogeneous enhancement in the mass (arrow). (c,d) DW imaging shows a hyperintense mass associated with decreased ADC (0.54×10^-3 mm²/s) that may reflect the hypercellularity of the central neurocytoma (arrow). (e) Pathology shows hypercellularity composed of small well-differentiated neurons with uniform nuclei.

![Fig. 8: Central Neurocytoma](image)
Fig. 9: Pineocytoma. (a) FLAIR. (b) Gadolinium-enhancement of the lesion. (c) DWI shows mild hyperintensity. (d) ADC map with value of 0.68-0.74x10^{-3} mm^2/s.

Fig. 10: Papillary tumor of the pineal region in an 18-year-old male patient. (a) T2-weighted image shows a well-defined mildly hyperintense lesion with a cystic component and fluid-fluid level (arrow). (b) Gadolinium-enhanced sagittal T1-weighted image shows heterogeneously enhancing lesions in the pineal and suprasellar regions and leptomeningeal enhancement along the cerebellum and spinal cord due to tumor
dissemination (arrows). (c) DW image shows a hyperintense lesion (arrow). (d) ADC map shows isointensity in the lesion (0.70-0.85×10^{-3} \text{mm}^2/\text{s}; arrow). (e) Micropathology specimen shows hypercellularity with a papillary growth pattern of plump epithelial-like cells and hemorrhage. Nuclei were uniform.
**Fig. 11:** Benign meningioma (meningothelial meningioma) in a 72-year-old woman with a visual disturbance. (a) T2-weighted image shows a slightly hyperintense mass near the frontal aspect of the falx. (b) Gadolinium-enhanced T1-weighted image shows homogeneous enhancement. (c) DW image shows hyperintensity in the lesion. (d) ADC map shows mild hypointensity (0.73-0.78×10^{-3} mm^2/s).

**Fig. 12:** Meningioma (microcystic meningioma) in a 68-year-old woman. (a) T2-weighted image shows a hyperintense mass in the left occipital region with no vasogenic edema. (b)
T1-weighted image shows a hypointense mass in the left occipital region. (c) Gadolinium-enhanced T1-weighted image with fat saturation shows a central heterogeneously enhancing mass (arrow) and peripheral microcystic components (arrowheads). (d) DW image shows a hyperintense mass (arrow) with peripheral hypointensity (arrowheads). (e) ADC map shows iso- or slight hypointensity centrally (arrow) with peripheral hyperintensity in the microcystic components (arrowheads). (f) FA map shows increased anisotropy in the central solid portion (arrow) and decreased anisotropy in the peripheral microcystic areas (arrowheads). (g) Pathology of the central portion shows spindle shaped tumor cells. (h) Pathology of the peripheral portion shows microcystic components.
Fig. 13: Atypical meningioma in a 45-year old female patient with headache. (a) T2-weighted image shows a heterogeneous intense mass in the temporal lobe (arrows). (b) Gadolinium-enhanced T1-weighted image shows heterogeneous enhancement
(arrows). (c) DW image shows heterogeneous hyperintensity (arrows). (d) ADC map shows hypointensity, especially in the right side of the mass (0.51×10^{-3} \text{ mm}^2/\text{s}; arrows)

Fig. 14: Hemangiopericytoma in a 50-year-old man. (a) T2-weighted image shows an extraaxial hyperintense mass involving the left parietal skull and scalp. (b) Gadolinium-enhanced T1-weighted image with fat saturation shows homogeneous enhancement with the dural tail. No adjacent hyperostosis or sclerotic changes are noted. (c) DW image shows mild hyperintensity. (d) ADC map shows decreased ADC of this mass. (e) Micropathology specimen shows hypercellularity, dense interstitium, and dilated thin-walled vessels
Fig. 15: Pituitary adenoma in a 62-year-old female patient. (a) Gadolinium-enhanced coronal T1-weighted image shows a homogeneously enhancing mass in the pituitary fossa involving the bilateral cavernous sinuses (arrows). (b,c) DW image shows hypointensity in the lesion and decreased ADC (0.46-0.77×10⁻³ mm²/s)
Fig. 16: Epidermoid tumor in a 9-year old girl without symptoms. (a) T2-weighted image shows a hyperintense mass near the falx. (b) T1-weighted image shows the hypointense lesion. (c) DW image shows hyperintensity in the lesion, which is caused by both increased T2 and restricted diffusivity. (d) ADC map shows heterogeneous iso- or
hypointensity in the lesion, consistent with restricted diffusion similar to that of the brain parenchyma
Conclusion

- Restricted diffusion was observed in not only malignant CNS neoplasms but also benign CNS neoplasms.
- Diffusion signals and ADC values of CNS neoplasms depend on their cellularity and components of the extracellular matrix.

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